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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,492	03/06/2002	Elizabeth S. Light	142/003/PCT	8768

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EXAMINER	
SWITZER, JULIET CAROLINE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,492	LIGHT ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004 and 04 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7,17,19 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,17,19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/28/04 and 8/4/04 has been entered.

2. The interview summary by applicant submitted 9/17/04 has been entered. The interview record is complete and correct.

3. Applicant's amendments filed 6/28/04 and 8/4/04 have been entered. Claims 1, 3, 7, 17, 19, and 22 have been amended and all other claims have been canceled. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The information disclosure statement filed 12/2/03 has been considered. A signed 1449 is enclosed with the office action.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 3, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Troncone *et al.* (J. Clin. Pathol. 1992, Vol. 45:308-313), as evidenced by Herrington *et al.* (J. Clin. Pathol. 1989 42:592-600).

Troncone *et al.* teach a reagent for detecting human papillomavirus DNA in a cell sample comprising a plurality of genomic DNA probe sets, wherein each probe set comprises a plurality of nucleic acid molecules that detectably hybridize to substantially all of the full length genomic sequence of HPV types 16, 18, and 33.

In particular, Troncone *et al.* teach a cocktail of genomic probes that were labeled with digoxigenin by nick translation (p. 309, "NISH ON CERVICAL SMEARS"). The process of nick translation inherently produces a set of nucleic acid probes that detectably hybridize to the translated target. Troncone *et al.* The probes taught by Troncone *et al.* are considered to hybridize to "substantially all" of the full length genomic sequence as evidenced by Herrington *et al.* Troncone *et al.* cite the Herrington *et al.* paper in reference to the labeling of the probes in the cocktail. Herrington *et al.* teach labeling of whole genomic HPV probes using nick translation. Therefore, the probe cocktail taught by Troncone *et al.* appears to meet all of the structural limitations of the claimed invention.

With regard to claim 3, the cross-hybridization of the probes taught by Troncone *et al.* to the genomic sequences of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 is an inherent property of the probes taught by Troncone *et al.* Some cross-hybridization of the full length probe cocktail taught by Troncone *et al.* to these sequences could be expected under some stringency conditions. Notably, this is evidenced by the instant specification which teaches that full length

nick translated genomic probe to HPV 18 hybridizes to 18, 39, 45, 56, 59, 68, and 70 and full length nick translated genomic probe to HPV 33 hybridizes to 16, 31, 33, 35, 45, 52, and 58.

With regard to claims 17 and 19, prior to application of the cocktail to the slide, the cocktail would inherently have been in a container.

Therefore, the cocktail provided by Troncone *et al.* anticipate the claimed invention.

7. Claims 1, 3, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Nuovo *et al.* (The Journal of Histotechnology, Vol. 8, No. 2, June 1995, p. 105-110).

Nuovo *et al.* teach a reagent for detecting human papillomavirus DNA in a cell sample comprising a plurality of genomic DNA probe sets, wherein each probe set comprises a plurality of nucleic acid molecules that detectably hybridize to substantially all of the full length genomic sequence of HPV types 16 and 18, as well as 31, 33, and 35. Nuovo *et al.* teach probe mixes provided by Digene that are made using teh entire genome and that contain probes for these groups of HPV subtypes (p. 106, "Probe selection.").

With regard to claim 3, the cross-hybridization of the probes taught by Nuovo *et al.* to the genomic sequences of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 is an inherent property of the probes taught by Nuovo *et al.* Some cross-hybridization of the full length probe cocktail taught by Nuovo *et al.* to these sequences could be expected under some stringency conditions. Notably, this is evidenced by the instant specification which teaches that full length nick translated genomic probe to HPV 18 hybridizes to 18, 39, 45, 56, 59, 68, and 70 and full length nick translated genomic probe to HPV 33 hybridizes to 16, 31, 33, 35, 45, 52, and 58.

With regard to claims 17 and 19, Nuovo *et al.* teach that they obtain these probes in kits from Digene Diagnostics, and these kits would inherently comprise containers containing the probes.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 3, 7, 17, 19, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 claims a reagent comprising a plurality of probe sets wherein each set comprises a plurality of nucleic acid molecules that detectably hybridize to substantially all of one of six recited HPV genomes. Therefore, claim 1 requires that the reagent comprise only two of the six groups of recited "plurality of nucleic acid molecules." While the specification exemplifies each individual set a plurality of nucleic acid molecules that detectably hybridize to substantially all of the full-length genomic sequences, and while the specification exemplifies a reagent that comprises all of the probe sets to all of HPV genomes 16, 18, 31, 33, 35 and 51, the specification does not appear to contemplate or disclose sets of any 2, 3, 4, or 5 of these which are encompassed by claim 1. Furthermore, as dependent upon claim 1, claim 3 contains new matter

because the specification does not contemplate pair wise sets of probes to the specific HPV genomes that also hybridize to HPV types 39, 45, 52, 56, 58, 59, 68, and 70. The specification only teaches a reagent that is a combination of a plurality of probes to all of those HPV genomes recited in claim 1 and also cross-hybridizes to the recited genomes.

Further, claim 3 contains new matter in the requirement that the claimed reagent hybridize to "substantially all of the full-length genomic sequence" of the HPV types recited in claim 3 because, though the specification teaches that the hybridization cocktail used in the examples detectably hybridizes to these genomes, it does not appear to teach how much of these genomes the probes hybridize to- i.e. the extent of the cross-hybridization along the length of these genomic sequences is not taught or discussed in the specification.

Claims 7, 17, 19, and 22 depend from claims 1 and 3 and therefore also contains these same issues of new matter.

Applicant's remarks filed 8/4/04 point to different portions of the specification for support for the amendments to the claims. However, as noted, each of these portions discuss or disclose either a reagent that comprises sets of probes to ALL of the HPV types recited in claim 1 or to the probes individually. Therefore, the claims are rejected as containing new matter.

10. Claims 3, 7, 19, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 3 and 7 the phrase "the genomic DNA HPV probes" lacks proper antecedent basis in claim 1 because the claim previously refers to "genomic HPV DNA probe sets" but

never to genomic DNA HPV probes and it is not clear if the claim intends to refer back to the probe sets recited in claim 1 or the plurality of nucleic acid molecules within an individual probe the probe sets.

Claim 7 is further indefinite because while the claim recites a particular percentage of each of the HPV types, it does not recite what the percentage is of total. For example, does the claim require that HPV 16 represent 8.3% of the total reagent? of a total probe mix? of a the amount of probe within a hybridization mix that might also contain other elements? A proportion is a part considered in reference to a whole, but the claim does not set forth what the whole is, so it is confusing.

Response to Remarks

Many of applicants remarks filed 6/28/04 are moot in view of the subsequently amended claims filed 8/4/04. Nonetheless, as the remarks may be relevant, they are addressed.

All previously set forth rejections that are not reiterated are withdrawn in view of either the amendment or cancellation of the relevant claims.

New grounds of rejection are set forth to address the amendments to the claims.

The Trocone *et al.* reference is applied to the amended claims, however, Applicant's remarks previously filed with regard to this reference are largely moot due to the amendments tot the claims. Applicants discuss whether or not the probe cocktail taught by Troncone *et al.* would hybridize to non-carcinogenic HPV types. This is not relevant with regard to the instant claims which do not have this requirement. Nonetheless, the fact remains, that Trocone *et al.* teach a cocktail of probes that comprises probes for HPV types 16, 18, and 33, each of which are carcinogenic HPV types.

Applicants contend that it is not clear from the reference that the 16/18/33 cocktail of Troncone *et al.* specifically hybridizes to only carcinogenic HPV types because in the samples that were tested using the cocktail, no non-carcinogenic HPV types were detected. This is not persuasive. First, the samples that were tested using the cocktail were not tested using probes to non-carcinogenic types. Thus, no detection was even possible. It is clear from the teachings of Troncone *et al.*, that they are using these probes to specifically detect the 16/18/33 types of HPV, and these are indisputably carcinogenic HPV types (as supported in fact by even applicant's own specification). Applicant does not provide any evidence that these probes would hybridize to non-carcinogenic types. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Applicant further argues that it is not clear that the probes used by Troncone *et al.* are genomic probes as opposed to oligonucleotide probes. However, this contention is addressed in the rejection herein. Namely, the Herrington *et al.* reference cited by Troncone *et al.* teaches that the probes were whole genomic probes made by nick translation. Furthermore, the teachings of Trocone *et al.* specifically teach that genomic probes are used in the NISH of histopathological samples, and it follows from the teaching that genomic probes are being used on the subsequently tested cervical smears, an argument that is supported by the fact that Trocone *et al.* utilize the same detection method on the smears and on the sections (p. 309, second column).

Conclusion

11. Claim 7 is free of the prior art because the prior art does not teach a reagent that has all of the recited genomic HPV DNA probes in the recited percentages. The claim is currently rejected for new matter and under 112 2nd paragraph. If these are overcome, the claim would be free of the prior art. It is further noted that the specification teaches an unexpected result wherein the HPV DNA probe sets for the subtypes recited in claim 7 are present in the percentages recited as percentage of TOTAL PROBE in the hybridization mixture. The unexpected result is the specificity with which this probe set is able to detect itself but also HPV of types 39, 45, 52, 56, 58, 59, 68, and 70.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Examiner
Art Unit 1634

October 18, 2004